GE11 positive exosomes as a potential RNAi delivery system in clear cell Renal Cell Carcinoma

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Aim: Use GE11 positive (GE11+) exosomes as a targeted delivery system to EGFR overexpressing cells for the treatment of clear cell Renal Cell Carcinoma (ccRCC).

Introduction: ccRCC is the most prevalent subtype of renal cancer and the most lethal urologic tumor. Generally, it is radio-chemotherapy resistant, and frequently associated with relapse after 5–11 months upon targeted therapy treatment, which highlight the need to develop new therapeutic strategies. Exosomes, extracellular vesicles of 40–150 nm that mediate intercellular communication, have emerged as promising therapeutic tools due to their engineering potential and ability to evade the immune system.

Methods: EGFR is known to be overexpressed in ccRCC thus, the expression of GE11, a peptide that binds to EGFR, in exosomes membrane enable a targeted delivery of therapeutic molecules to EGFR overexpressing cells. Exosomes derived from HEK293T were engineered to express the GE11 peptide on their surface and incubated with normal or tumor renal cell lines.

Results: Our results revealed EGFR overexpression at the mRNA and protein levels in a ccRCC cell line, compared to a normal renal cell line. Furthermore, tumor cells presented increased protein levels of phosphorylated EGFR when compared to normal cells. These results support the hypothesis of using an EGFR-based exosomes delivery model, the GE11+ exosomes. A higher percentage of tumor cells internalized GE11+ exosomes compared to exosomes derived from HEK293T cells transfected with control condition. Additionally, tumor cells exhibited an increased mean of fluorescence intensity compared to the control, suggesting that each cell uptakes more GE11+ exosomes in an EGFR-dependent manner. Importantly, GE11+ exosomes were internalized in a greater proportion by tumor cells rather than normal renal cell lines.

Conclusion: Overall, the use of GE11+ exosomes as a new delivery system is a promising therapeutic strategy for ccRCC treatment. Ultimately, these exosomes can be loaded with RNAi-based drugs to target deregulated genes in ccRCC.